

SEQUENCE LISTING

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- <120> MODULATORS OF NOTCH SIGNALLING FOR USE IN IMMUNOTHERAPY
- <130> 674525-2010
- <140> 10/765,727
- <141> 2004-01-23
- <150> PCT/GB02/03426
- <151> 2002-07-25
- <150> GB 0118153.6
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- <150> GB 0207930.9
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- <160> 40
- <170> PatentIn Ver. 3.2
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- <212> PRT
- <213> Drosophila melanogaster
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- Phe Arg Val Thr Cys Asp Leu Asn Tyr Tyr Gly Ser Gly Cys Ala Lys 20 25 30
- Phe Cys Arg Pro Arg Asp Asp Ser Phe Gly His Ser Thr Cys Ser Glu 35 40 45
- Thr Gly Glu Ile Ile Cys Leu Thr Gly Trp Gln Gly Asp Tyr Cys 50 $$ 55 $$ 60 $$
- <210> 2
- <211> 63
- <212> PRT
- <213> Homo sapiens

Trp Ser Gln Asp Leu His Ser Ser Gly Arg Thr Asp Leu Lys Tyr Ser 1 5 10 15

Tyr Arg Phe Val Cys Asp Glu His Tyr Tyr Gly Glu Gly Cys Ser Val 20 25 30

Phe Cys Arg Pro Arg Asp Asp Ala Phe Gly His Phe Thr Cys Gly Glu 35 40 45

Arg Gly Glu Lys Val Cys Asn Pro Gly Trp Lys Gly Pro Tyr Cys
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<210> 3

<211> 63

<212> PRT

<213> Mus musculus

<400> 3

Trp Ser Gln Asp Leu His Ser Ser Gly Arg Thr Asp Leu Arg Tyr Ser $\mathbf{1}^{-}$ 5 10 15

Tyr Arg Phe Val Cys Asp Glu His Tyr Tyr Gly Glu Gly Cys Ser Val 20 25 30

Phe Cys Arg Pro Arg Asp Asp Ala Phe Gly His Phe Thr Cys Gly Asp 35 40 45

Arg Gly Glu Lys Met Cys Asp Pro Gly Trp Lys Gly Gln Tyr Cys
50 55 60

<210> 4

<211> 63

<212> PRT

<213> Rattus norvegicus

<400> 4

Trp Ser Gln Asp Leu His Ser Ser Gly Arg Thr Asp Leu Arg Tyr Ser 1 5 10 15

Tyr Arg Phe Val Cys Asp Glu His Tyr Tyr Gly Glu Gly Cys Ser Val 20 25 30

Phe Cys Arg Pro Arg Asp Asp Ala Phe Gly His Phe Thr Cys Gly Glu
35 40 45

Arg Gly Glu Lys Met Cys Asp Pro Gly Trp Lys Gly Gln Tyr Cys
50 55 60

<210> 5

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<212> PRT

<213> Mus musculus

Trp Arg Thr Asp Glu Gln Asn Asp Thr Leu Thr Arg Leu Ser Tyr Ser 1 5 10 15

Tyr Arg Val Ile Cys Ser Asp Asn Tyr Tyr Gly Glu Ser Cys Ser Arg 20 25 30

Leu Cys Lys Lys Arg Asp Asp His Phe Gly His Tyr Glu Cys Gln Pro 35 40 45

Asp Gly Ser Leu Ser Cys Leu Pro Gly Trp Thr Gly Lys Tyr Cys 50 55 60

<210> 6

<211> 63

<212> PRT

<213> Homo sapiens

<400> 6

Trp Leu Leu Asp Glu Gln Thr Ser Thr Leu Thr Arg Leu Arg Tyr Ser 1 5 10 15

Tyr Arg Val Ile Cys Ser Asp Asn Tyr Tyr Gly Asp Asn Cys Ser Arg
20 25 30

Leu Cys Lys Lys Arg Asn Asp His Phe Gly His Tyr Val Cys Gln Pro 35 40 45

Asp Gly Asn Leu Ser Cys Leu Pro Gly Trp Thr Gly Glu Tyr Cys
50 55 60

<210> 7

<211> 63

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<213> Rattus norvegicus

<400> 7

Trp Gln Thr Leu Lys Gln Asn Thr Gly Ile Ala His Phe Glu Tyr Gln 1 5 10 15

Ile Arg Val Thr Cys Asp Asp His Tyr Tyr Gly Phe Gly Cys Asn Lys 20 25 30

Phe Cys Arg Pro Arg Asp Asp Phe Phe Gly His Tyr Ala Cys Asp Gln 35 40 45

Asn Gly Asn Lys Thr Cys Met Glu Gly Trp Met Gly Pro Glu Cys
50 55 60

<210> 8

<211> 63

<212> PRT

<213> Mus musculus

Trp Gln Thr Leu Lys Gln Asn Thr Gly Ile Ala His Phe Glu Tyr Gln
1 5 10 15

Ile Arg Val Thr Cys Asp Asp His Tyr Tyr Gly Phe Gly Cys Asn Lys
20 25 30

Phe Cys Arg Pro Arg Asp Asp Phe Phe Gly His Tyr Ala Cys Asp Gln 35 40 45

Asn Gly Asn Lys Thr Cys Met Glu Gly Trp Met Gly Pro Asp Cys 50 55 60

<210> 9

<211> 63

<212> PRT

<213> Homo sapiens

<400> 9

Trp Gln Thr Leu Lys Gln Asn Thr Gly Val Ala His Phe Glu Tyr Gln
1 10 15

Ile Arg Val Thr Cys Asp Asp Tyr Tyr Tyr Gly Phe Gly Cys Asn Lys
20 25 30

Phe Cys Arg Pro Arg Asp Asp Phe Phe Gly His Tyr Ala Cys Asp Gln 35 40 45

Asn Gly Asn Lys Thr Cys Met Glu Gly Trp Met Gly Arg Glu Cys 50 60

<210> 10

<211> 63

<212> PRT

<213> Gallus gallus

<400> 10

Trp Gln Thr Leu Lys His Asn Thr Gly Ala Ala His Phe Glu Tyr Gln
1 10 15

Ile Arg Val Thr Cys Ala Glu His Tyr Tyr Gly Phe Gly Cys Asn Lys
20 25 30

Phe Cys Arg Pro Arg Asp Asp Phe Phe Thr His His Thr Cys Asp Gln 35 40 45

Asn Gly Asn Lys Thr Cys Leu Glu Gly Trp Thr Gly Pro Glu Cys 50 55 60

<210> 11

<211> 63

<212> PRT

<213> Gallus gallus

Trp Lys Thr Leu Gln Phe Asn Gly Pro Val Ala Asn Phe Glu Val Gln
1 5 10 15

Ile Arg Val Lys Cys Asp Glu Asn Tyr Tyr Ser Ala Leu Cys Asn Lys
20 25 30

Phe Cys Gly Pro Arg Asp Asp Phe Val Gly His Tyr Thr Cys Asp Gln 35 40 45

Asn Gly Asn Lys Ala Cys Met Glu Gly Trp Met Gly Glu Glu Cys
50 55 60

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<211> 63

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<213> Mus musculus

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Trp Lys Ser Leu His Phe Ser Gly His Val Ala His Leu Glu Leu Gln 1 5 10 15

Ile Arg Val Arg Cys Asp Glu Asn Tyr Tyr Ser Ala Thr Cys Asn Lys
20 25 30

Phe Cys Arg Pro Arg Asn Asp Phe Phe Gly His Tyr Thr Cys Asp Gln 35 40 45

Tyr Gly Asn Lys Ala Cys Met Asp Gly Trp Met Gly Lys Glu Cys
50 55 60

<210> 13

<211> 63

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<213> Homo sapiens

<400> 13

Trp Lys Ser Leu His Phe Ser Gly His Val Ala His Leu Glu Leu Gln 1 5 10 15

Ile Arg Val Arg Cys Asp Glu Asn Tyr Tyr Ser Ala Thr Cys Asn Lys 20 25 30

Phe Cys Arg Pro Arg Asn Asp Phe Phe Gly His Tyr Thr Cys Asp Gln

Tyr Gly Asn Lys Ala Cys Met Asp Gly Trp Met Gly Lys Glu Cys
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<210> 14

<211> 63

<212> PRT

<213> Rattus norvegicus

Trp Lys Ser Leu His Phe Ser Gly His Val Ala His Leu Glu Leu Gln 1 5 10 15

Ile Arg Val Arg Cys Asp Glu Asn Tyr Tyr Ser Ala Thr Cys Asn Lys
20 25 30

Phe Cys Arg Pro Arg Asn Asp Phe Phe Gly His Tyr Thr Cys Asp Gln 35 40 45

Tyr Gly Asn Lys Ala Cys Met Asp Gly Trp Met Gly Lys Glu Cys 50 55 60

<210> 15

<211> 63

<212> PRT

<213> Homo sapiens

<400> 15

Trp Lys Ser Leu His Phe Ser Gly His Val Ala His Leu Glu Leu Gln 1 5 10 15

Ile Arg Val Arg Cys Asp Glu Asn Tyr Tyr Ser Ala Thr Cys Asn Lys
20 25 30

Phe Cys Arg Pro Arg Asn Asp Phe Phe Gly His Tyr Thr Cys Asp Gln 35 40 45

Tyr Gly Asn Lys Ala Cys Met Asp Gly Trp Met Gly Lys Glu Cys 50 55 60

<210> 16

<211> 63

<212> PRT

<213> Drosophila melanogaster

<400> 16

Trp Lys Thr Leu Asp His Ile Gly Arg Asn Ala Arg Ile Thr Tyr Arg 1 5 10 15

Val Arg Val Gln Cys Ala Val Thr Tyr Tyr Asn Thr Thr Cys Thr Thr
20 25 30

Phe Cys Arg Pro Arg Asp Asp Gln Phe Gly His Tyr Ala Cys Gly Ser 35 40 45

Glu Gly Gln Lys Leu Cys Leu Asn Gly Trp Gln Gly Val Asn Cys
50 55 60

<210> 17

<211> 723

<212> PRT

<213> Homo sapiens

<400> 17 Met Gly Ser Arg Cys Ala Leu Ala Leu Ala Val Leu Ser Ala Leu Leu Cys Gln Val Trp Ser Ser Gly Val Phe Glu Leu Lys Leu Gln Glu Phe Val Asn Lys Lys Gly Leu Leu Gly Asn Arg Asn Cys Cys Arg Gly Gly Ala Gly Pro Pro Pro Cys Ala Cys Arg Thr Phe Phe Arg Val Cys Leu Lys His Tyr Gln Ala Ser Val Ser Pro Glu Pro Pro Cys Thr Tyr Gly Ser Ala Val Thr Pro Val Leu Gly Val Asp Ser Phe Ser Leu Pro Asp Gly Gly Ala Asp Ser Ala Phe Ser Asn Pro Ile Arg Phe Pro Phe 105 Gly Phe Thr Trp Pro Gly Thr Phe Ser Leu Ile Ile Glu Ala Leu His 120 Thr Asp Ser Pro Asp Asp Leu Ala Thr Glu Asn Pro Glu Arg Leu Ile 135 Ser Arg Leu Ala Thr Gln Arg His Leu Thr Val Gly Glu Glu Trp Ser 150 155 Gln Asp Leu His Ser Ser Gly Arg Thr Asp Leu Lys Tyr Ser Tyr Arg Phe Val Cys Asp Glu His Tyr Tyr Gly Glu Gly Cys Ser Val Phe Cys 185 Arg Pro Arg Asp Asp Ala Phe Gly His Phe Thr Cys Gly Glu Arg Gly 200 Glu Lys Val Cys Asn Pro Gly Trp Lys Gly Pro Tyr Cys Thr Glu Pro Ile Cys Leu Pro Gly Cys Asp Glu Gln His Gly Phe Cys Asp Lys Pro Gly Glu Cys Lys Cys Arg Val Gly Trp Gln Gly Arg Tyr Cys Asp Glu Cys Ile Arg Tyr Pro Gly Cys Leu His Gly Thr Cys Gln Gln Pro Trp 265 Gln Cys Asn Cys Gln Glu Gly Trp Gly Gly Leu Phe Cys Asn Gln Asp Leu Asn Tyr Cys Thr His His Lys Pro Cys Lys Asn Gly Ala Thr Cys

Thr Asn Thr Gly Gln Gly Ser Tyr Thr Cys Ser Cys Arg Pro Gly Tyr Thr Gly Ala Thr Cys Glu Leu Gly Ile Asp Glu Cys Asp Pro Ser Pro Cys Lys Asn Gly Gly Ser Cys Thr Asp Leu Glu Asn Ser Tyr Ser Cys 345 Thr Cys Pro Pro Gly Phe Tyr Gly Lys Ile Cys Glu Leu Ser Ala Met Thr Cys Ala Asp Gly Pro Cys Phe Asn Gly Gly Arg Cys Ser Asp Ser Pro Asp Gly Gly Tyr Ser Cys Arg Cys Pro Val Gly Tyr Ser Gly Phe Asn Cys Glu Lys Lys Ile Asp Tyr Cys Ser Ser Ser Pro Cys Ser Asn 410 Gly Ala Lys Cys Val Asp Leu Gly Asp Ala Tyr Leu Cys Arg Cys Gln Ala Gly Phe Ser Gly Arg His Cys Asp Asp Asn Val Asp Asp Cys Ala Ser Ser Pro Cys Ala Asn Gly Gly Thr Cys Arg Asp Gly Val Asn Asp Phe Ser Cys Thr Cys Pro Pro Gly Tyr Thr Gly Arg Asn Cys Ser Ala Pro Val Ser Arg Cys Glu His Ala Pro Cys His Asn Gly Ala Thr Cys His Glu Arg Gly His Gly Tyr Val Cys Glu Cys Ala Arg Gly Tyr Gly Gly Pro Asn Cys Gln Phe Leu Leu Pro Glu Leu Pro Pro Gly Pro Ala 520 Val Val Asp Leu Thr Glu Lys Leu Glu Gly Gln Gly Gly Pro Phe Pro Trp Val Ala Val Cys Ala Gly Val Ile Leu Val Leu Met Leu Leu Gly Cys Ala Ala Val Val Cys Val Arg Leu Arg Leu Gln Lys His 570 Arg Pro Pro Ala Asp Pro Cys Arg Gly Glu Thr Glu Thr Met Asn Asn Leu Ala Asn Cys Gln Arg Glu Lys Asp Ile Ser Val Ser Ile Ile Gly

600

605

Ala Thr Gln Ile Lys Asn Thr Asn Lys Lys Ala Asp Phe His Gly Asp 610 620

His Ser Ala Asp Lys Asn Gly Phe Lys Ala Arg Tyr Pro Ala Val Asp 625 630 635 640

Tyr Asn Leu Val Gln Asp Leu Lys Gly Asp Asp Thr Ala Val Arg Asp 645 650 655

Ala His Ser Lys Arg Asp Thr Lys Cys Gln Pro Gln Gly Ser Ser Gly 660 665 670

Glu Glu Lys Gly Thr Pro Thr Thr Leu Arg Gly Gly Glu Ala Ser Glu 675 680 685

Arg Lys Arg Pro Asp Ser Gly Cys Ser Thr Ser Lys Asp Thr Lys Tyr 690 695 700

Gln Ser Val Tyr Val Ile Ser Glu Glu Lys Asp Glu Cys Val Ile Ala 705 710 715 720

Thr Glu Val

<210> 18

<211> 618

<212> PRT

<213> Homo sapiens

<400> 18

Met Val Ser Pro Arg Met Ser Gly Leu Leu Ser Gln Thr Val Ile Leu 1 5 10 15

Ala Leu Ile Phe Leu Pro Gln Thr Arg Pro Ala Gly Val Phe Glu Leu 20 25 30

Gln Ile His Ser Phe Gly Pro Gly Pro Gly Pro Gly Ala Pro Arg Ser 35 40 45

Pro Cys Ser Ala Arg Leu Pro Cys Arg Leu Phe Phe Arg Val Cys Leu 50 60

Lys Pro Gly Leu Ser Glu Glu Ala Ala Glu Ser Pro Cys Ala Leu Gly 65 70 75 80

Ala Ala Leu Ser Ala Arg Gly Pro Val Tyr Thr Glu Gln Pro Gly Ala 85 90 95

Pro Ala Pro Asp Leu Pro Leu Pro Asp Gly Leu Leu Gln Val Pro Phe
100 105 110

Arg Asp Ala Trp Pro Gly Thr Phe Ser Phe Ile Ile Glu Thr Trp Arg 115 120 125

Glu Glu Leu Gly Asp Gln Ile Gly Gly Pro Ala Trp Ser Leu Leu Ala Arg Val Ala Gly Arg Arg Leu Ala Ala Gly Gly Pro Trp Ala Arg Asp Ile Gln Arg Ala Gly Ala Trp Glu Leu Arg Phe Ser Tyr Arg Ala Arg Cys Glu Pro Pro Ala Val Gly Thr Ala Cys Thr Arg Leu Cys Arg 185 Pro Arg Ser Ala Pro Ser Arg Cys Gly Pro Gly Leu Arg Pro Cys Ala Pro Leu Glu Asp Glu Cys Glu Ala Pro Leu Val Cys Arg Ala Gly Cys Ser Pro Glu His Gly Phe Cys Glu Gln Pro Gly Glu Cys Arg Cys Leu 230 Glu Gly Trp Thr Gly Pro Leu Cys Thr Val Pro Val Ser Thr Ser Ser 250 Cys Leu Ser Pro Arg Gly Pro Ser Ser Ala Thr Thr Gly Cys Leu Val 265 Pro Gly Pro Gly Pro Cys Asp Gly Asn Pro Cys Ala Asn Gly Gly Ser Cys Ser Glu Thr Pro Arg Ser Phe Glu Cys Thr Cys Pro Arg Gly Phe 295 Tyr Gly Leu Arg Cys Glu Val Ser Gly Val Thr Cys Ala Asp Gly Pro Cys Phe Asn Gly Gly Leu Cys Val Gly Gly Ala Asp Pro Asp Ser Ala Tyr Ile Cys His Cys Pro Pro Gly Phe Gln Gly Ser Asn Cys Glu Lys Arg Val Asp Arg Cys Ser Leu Gln Pro Cys Arg Asn Gly Gly Leu Cys 360 Leu Asp Leu Gly His Ala Leu Arg Cys Arg Cys Arg Ala Gly Phe Ala 375 Gly Pro Arg Cys Glu His Asp Leu Asp Asp Cys Ala Gly Arg Ala Cys Ala Asn Gly Gly Thr Cys Val Glu Gly Gly Ala His Arg Cys Ser 405 Cys Ala Leu Gly Phe Gly Gly Arg Asp Cys Arg Glu Arg Ala Asp Pro 425 430

Cys Ala Ala Arg Pro Cys Ala His Gly Gly Arg Cys Tyr Ala His Phe 435 440 445

Ser Gly Leu Val Cys Ala Cys Ala Pro Gly Tyr Met Gly Ala Arg Cys 450 450 460

Glu Phe Pro Val His Pro Asp Gly Ala Ser Ala Leu Pro Ala Ala Pro 465 470 475 480

Pro Gly Leu Arg Pro Gly Asp Pro Gln Arg Tyr Leu Leu Pro Pro Ala 485 490 495

Leu Gly Leu Leu Val Ala Ala Gly Val Ala Gly Ala Ala Leu Leu Leu 500 505 510

Val His Val Arg Arg Gly His Ser Gln Asp Ala Gly Ser Arg Leu 515 520 525

Leu Ala Gly Thr Pro Glu Pro Ser Val His Ala Leu Pro Asp Ala Leu 530 535 540

Asn Asn Leu Arg Thr Gln Glu Gly Ser Gly Asp Gly Pro Ser Ser Ser 545 550 555

Val Asp Trp Asn Arg Pro Glu Asp Val Asp Pro Gln Gly Ile Tyr Val
565 570 575

Ile Ser Ala Pro Ser Ile Tyr Ala Arg Glu Val Ala Thr Pro Leu Phe 580 585 590

Pro Pro Leu His Thr Gly Arg Ala Gly Gln Arg Gln His Leu Leu Phe 595 600 605

Pro Tyr Pro Ser Ser Ile Leu Ser Val Lys 610 615

<210> 19

<211> 685

<212> PRT

<213> Homo sapiens

<400> 19

Met Ala Ala Ser Arg Ser Ala Ser Gly Trp Ala Leu Leu Leu 1 5 10 15

Val Ala Leu Trp Gln Gln Arg Ala Ala Gly Ser Gly Val Phe Gln Leu 20 25 30

Gln Leu Gln Glu Phe Ile Asn Glu Arg Gly Val Leu Ala Ser Gly Arg 35 40 45

Pro Cys Glu Pro Gly Cys Arg Thr Phe Phe Arg Val Cys Leu Lys His 50 55 60

Phe Gln Ala Val Val Ser Pro Gly Pro Cys Thr Phe Gly Thr Val Ser 65 70 75 80

Thr Pro Val Leu Gly Thr Asn Ser Phe Ala Val Arg Asp Asp Ser Ser Gly Gly Gly Arg Asn Pro Leu Gln Leu Pro Phe Asn Phe Thr Trp Pro Gly Thr Phe Ser Leu Ile Ile Glu Ala Trp His Ala Pro Gly Asp Asp 120 Leu Arg Pro Glu Ala Leu Pro Pro Asp Ala Leu Ile Ser Lys Ile Ala 135 Ile Gln Gly Ser Leu Ala Val Gly Gln Asn Trp Leu Leu Asp Glu Gln 155 Thr Ser Thr Leu Thr Arg Leu Arg Tyr Ser Tyr Arg Val Ile Cys Ser Asp Asn Tyr Tyr Gly Asp Asn Cys Ser Arg Leu Cys Lys Lys Arg Asn 185 Asp His Phe Gly His Tyr Val Cys Gln Pro Asp Gly Asn Leu Ser Cys Leu Pro Gly Trp Thr Gly Glu Tyr Cys Gln Gln Pro Ile Cys Leu Ser Gly Cys His Glu Gln Asn Gly Tyr Cys Ser Lys Pro Ala Glu Cys Leu 230 235 Cys Arg Pro Gly Trp Gln Gly Arg Leu Cys Asn Glu Cys Ile Pro His Asn Gly Cys Arg His Gly Thr Cys Ser Thr Pro Trp Gln Cys Thr Cys 265 Asp Glu Gly Trp Gly Gly Leu Phe Cys Asp Gln Asp Leu Asn Tyr Cys Thr His His Ser Pro Cys Lys Asn Gly Ala Thr Cys Ser Asn Ser Gly Gln Arg Ser Tyr Thr Cys Thr Cys Arg Pro Gly Tyr Thr Gly Val Asp Cys Glu Leu Glu Leu Ser Glu Cys Asp Ser Asn Pro Cys Arg Asn Gly Gly Ser Cys Lys Asp Gln Glu Asp Gly Tyr His Cys Leu Cys Pro Pro Gly Tyr Tyr Gly Leu His Cys Glu His Ser Thr Leu Ser Cys Ala Asp Ser Pro Cys Phe Asn Gly Gly Ser Cys Arg Glu Arg Asn Gln Gly Ala

375

Asn Tyr Ala Cys Glu Cys Pro Pro Asn Phe Thr Gly Ser Asn Cys Glu 395 Lys Lys Val Asp Arg Cys Thr Ser Asn Pro Cys Ala Asn Gly Gly Gln Cys Leu Asn Arg Gly Pro Ser Arg Met Cys Arg Cys Arg Pro Gly Phe 425 Thr Gly Thr Tyr Cys Glu Leu His Val Ser Asp Cys Ala Arg Asn Pro Cys Ala His Gly Gly Thr Cys His Asp Leu Glu Asn Gly Leu Met Cys Thr Cys Pro Ala Gly Phe Ser Gly Arg Arg Cys Glu Val Arg Thr Ser Ile Asp Ala Cys Ala Ser Ser Pro Cys Phe Asn Arg Ala Thr Cys Tyr 490 Thr Asp Leu Ser Thr Asp Thr Phe Val Cys Asn Cys Pro Tyr Gly Phe 505 Val Gly Ser Arg Cys Glu Phe Pro Val Gly Leu Pro Pro Ser Phe Pro Trp Val Ala Val Ser Leu Gly Val Gly Leu Ala Val Leu Leu Val Leu 535 Leu Gly Met Val Ala Val Ala Val Arg Gln Leu Arg Leu Arg Arg Pro Asp Asp Gly Ser Arg Glu Ala Met Asn Asn Leu Ser Asp Phe Gln Lys 570 Asp Asn Leu Ile Pro Ala Ala Gln Leu Lys Asn Thr Asn Gln Lys Lys 580 Glu Leu Glu Val Asp Cys Gly Leu Asp Lys Ser Asn Cys Gly Lys Gln 600 Gln Asn His Thr Leu Asp Tyr Asn Leu Ala Pro Gly Pro Leu Gly Arg Gly Thr Met Pro Gly Lys Phe Pro His Ser Asp Lys Ser Leu Gly Glu Lys Ala Pro Leu Arg Leu His Ser Glu Lys Pro Glu Cys Arg Ile Ser 650 Ala Ile Cys Ser Pro Arg Asp Ser Met Tyr Gln Ser Val Cys Leu Ile 670 Ser Glu Glu Arg Asn Glu Cys Val Ile Ala Thr Glu Val

680

<210> 20

<211> 1218

<212> PRT

<213> Homo sapiens

<400> 20

Met Arg Ser Pro Arg Thr Arg Gly Arg Ser Gly Arg Pro Leu Ser Leu $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Leu Leu Ala Leu Cys Ala Leu Arg Ala Lys Val Cys Gly Ala Ser 20 25 30

Gly Gln Phe Glu Leu Glu Ile Leu Ser Met Gln Asn Val Asn Gly Glu 35 40 45

Leu Gln Asn Gly Asn Cys Cys Gly Gly Ala Arg Asn Pro Gly Asp Arg 50 55 60

Lys Cys Thr Arg Asp Glu Cys Asp Thr Tyr Phe Lys Val Cys Leu Lys 65 70 75 80

Glu Tyr Gln Ser Arg Val Thr Ala Gly Gly Pro Cys Ser Phe Gly Ser 85 90 95

Gly Ser Thr Pro Val Ile Gly Gly Asn Thr Phe Asn Leu Lys Ala Ser 100 105 110

Arg Gly Asn Asp Arg Asn Arg Ile Val Leu Pro Phe Ser Phe Ala Trp 115 120 125

Pro Arg Ser Tyr Thr Leu Leu Val Glu Ala Trp Asp Ser Ser Asn Asp 130 135 140

Thr Val Gln Pro Asp Ser Ile Ile Glu Lys Ala Ser His Ser Gly Met 145 150 155 160

Ile Asn Pro Ser Arg Gln Trp Gln Thr Leu Lys Gln Asn Thr Gly Val 165 170 175

Ala His Phe Glu Tyr Gln Ile Arg Val Thr Cys Asp Asp Tyr Tyr 180 185 190

Gly Phe Gly Cys Asn Lys Phe Cys Arg Pro Arg Asp Asp Phe Phe Gly 195 200 205

His Tyr Ala Cys Asp Gln Asn Gly Asn Lys Thr Cys Met Glu Gly Trp 210 215 220

Met Gly Pro Glu Cys Asn Arg Ala Ile Cys Arg Gln Gly Cys Ser Pro 225 230 235 240

Lys His Gly Ser Cys Lys Leu Pro Gly Asp Cys Arg Cys Gln Tyr Gly 245 250 255

Trp Gln Gly Leu Tyr Cys Asp Lys Cys Ile Pro His Pro Gly Cys Val His Gly Ile Cys Asn Glu Pro Trp Gln Cys Leu Cys Glu Thr Asn Trp Gly Gly Gln Leu Cys Asp Lys Asp Leu Asn Tyr Cys Gly Thr His Gln 290 295 Pro Cys Leu Asn Gly Gly Thr Cys Ser Asn Thr Gly Pro Asp Lys Tyr Gln Cys Ser Cys Pro Glu Gly Tyr Ser Gly Pro Asn Cys Glu Ile Ala Glu His Ala Cys Leu Ser Asp Pro Cys His Asn Arg Gly Ser Cys Lys Glu Thr Ser Leu Gly Phe Glu Cys Glu Cys Ser Pro Gly Trp Thr Gly Pro Thr Cys Ser Thr Asn Ile Asp Asp Cys Ser Pro Asn Asn Cys Ser His Gly Gly Thr Cys Gln Asp Leu Val Asn Gly Phe Lys Cys Val Cys Pro Pro Gln Trp Thr Gly Lys Thr Cys Gln Leu Asp Ala Asn Glu Cys 405 Glu Ala Lys Pro Cys Val Asn Ala Lys Ser Cys Lys Asn Leu Ile Ala Ser Tyr Tyr Cys Asp Cys Leu Pro Gly Trp Met Gly Gln Asn Cys Asp Ile Asn Ile Asn Asp Cys Leu Gly Gln Cys Gln Asn Asp Ala Ser Cys Arg Asp Leu Val Asn Gly Tyr Arg Cys Ile Cys Pro Pro Gly Tyr Ala 470 Gly Asp His Cys Glu Arg Asp Ile Asp Glu Cys Ala Ser Asn Pro Cys Leu Asn Gly Gly His Cys Gln Asn Glu Ile Asn Arg Phe Gln Cys Leu 505 Cys Pro Thr Gly Phe Ser Gly Asn Leu Cys Gln Leu Asp Ile Asp Tyr 515 520 Cys Glu Pro Asn Pro Cys Gln Asn Gly Ala Gln Cys Tyr Asn Arg Ala 535 Ser Asp Tyr Phe Cys Lys Cys Pro Glu Asp Tyr Glu Gly Lys Asn Cys 555

Ser His Leu Lys Asp His Cys Arg Thr Thr Pro Cys Glu Val Ile Asp Ser Cys Thr Val Ala Met Ala Ser Asn Asp Thr Pro Glu Gly Val Arg 585 Tyr Ile Ser Ser Asn Val Cys Gly Pro His Gly Lys Cys Lys Ser Gln 600 Ser Gly Gly Lys Phe Thr Cys Asp Cys Asn Lys Gly Phe Thr Gly Thr Tyr Cys His Glu Asn Ile Asn Asp Cys Glu Ser Asn Pro Cys Arg Asn Gly Gly Thr Cys Ile Asp Gly Val Asn Ser Tyr Lys Cys Ile Cys Ser Asp Gly Trp Glu Gly Ala Tyr Cys Glu Thr Asn Ile Asn Asp Cys Ser 665 Gln Asn Pro Cys His Asn Gly Gly Thr Cys Arg Asp Leu Val Asn Asp Phe Tyr Cys Asp Cys Lys Asn Gly Trp Lys Gly Lys Thr Cys His Ser Arg Asp Ser Gln Cys Asp Glu Ala Thr Cys Asn Asn Gly Gly Thr Cys 710 715 Tyr Asp Glu Gly Asp Ala Phe Lys Cys Met Cys Pro Gly Gly Trp Glu Gly Thr Thr Cys Asn Ile Ala Arg Asn Ser Ser Cys Leu Pro Asn Pro Cys His Asn Gly Gly Thr Cys Val Val Asn Gly Glu Ser Phe Thr Cys Val Cys Lys Glu Gly Trp Glu Gly Pro Ile Cys Ala Gln Asn Thr Asn Asp Cys Ser Pro His Pro Cys Tyr Asn Ser Gly Thr Cys Val Asp Gly Asp Asn Trp Tyr Arg Cys Glu Cys Ala Pro Gly Phe Ala Gly Pro Asp Cys Arg Ile Asn Ile Asn Glu Cys Gln Ser Ser Pro Cys Ala Phe Gly 820 825 Ala Thr Cys Val Asp Glu Ile Asn Gly Tyr Arg Cys Val Cys Pro Pro Gly His Ser Gly Ala Lys Cys Gln Glu Val Ser Gly Arg Pro Cys Ile

- Thr Met Gly Ser Val Ile Pro Asp Gly Ala Lys Trp Asp Asp Asp Cys 865 870 875 880
- Asn Thr Cys Gln Cys Leu Asn Gly Arg Ile Ala Cys Ser Lys Val Trp 885 890 895
- Cys Gly Pro Arg Pro Cys Leu Leu His Lys Gly His Ser Glu Cys Pro 900 905 910
- Ser Gly Gln Ser Cys Ile Pro Ile Leu Asp Asp Gln Cys Phe Val His 915 920 925
- Pro Cys Thr Gly Val Gly Glu Cys Arg Ser Ser Ser Leu Gln Pro Val 930 940
- Lys Thr Lys Cys Thr Ser Asp Ser Tyr Tyr Gln Asp Asn Cys Ala Asn 945 950 955 960
- Ile Thr Phe Thr Phe Asn Lys Glu Met Met Ser Pro Gly Leu Thr Thr
 965 970 975
- Glu His Ile Cys Ser Glu Leu Arg Asn Leu Asn Ile Leu Lys Asn Val 980 985 990
- Ser Ala Glu Tyr Ser Ile Tyr Ile Ala Cys Glu Pro Ser Pro Ser Ala 995 1000 1005
- Asn Asn Glu Ile His Val Ala Ile Ser Ala Glu Asp Ile Arg Asp Asp 1010 1015 1020
- Gly Asn Pro Ile Lys Glu Ile Thr Asp Lys Ile Ile Asp Leu Val Ser 1025 1030 1035 1040
- Lys Arg Asp Gly Asn Ser Ser Leu Ile Ala Ala Val Ala Glu Val Arg 1045 1050 1055
- Val Gln Arg Arg Pro Leu Lys Asn Arg Thr Asp Phe Leu Val Pro Leu 1060 1065 1070
- Leu Ser Ser Val Leu Thr Val Ala Trp Ile Cys Cys Leu Val Thr Ala 1075 1080 1085
- Phe Tyr Trp Cys Leu Arg Lys Arg Lys Pro Gly Ser His Thr His 1090 1095 1100
- Ser Ala Ser Glu Asp Asn Thr Thr Asn Asn Val Arg Glu Gln Leu Asn 1105 1110 1115 1120
- Gln Ile Lys Asn Pro Ile Glu Lys His Gly Ala Asn Thr Val Pro Ile 1125 1130 1135
- Lys Asp Tyr Glu Asn Lys Asn Ser Lys Met Ser Lys Ile Arg Thr His 1140 \$1145\$ 1150
- Asn Ser Glu Val Glu Glu Asp Asp Met Asp Lys His Gln Gln Lys Ala 1155 1160 1165

Arg Phe Ala Lys Gln Pro Ala Tyr Thr Leu Val Asp Arg Glu Glu Lys 1170 1175 1180

Pro Pro Asn Gly Thr Pro Thr Lys His Pro Asn Trp Thr Asn Lys Gln 1185 1190 1195 1200

Asp Asn Arg Asp Leu Glu Ser Ala Gln Ser Leu Asn Arg Met Glu Tyr 1205 1210 1215

Ile Val

<210> 21

<211> 1238

<212> PRT

<213> Homo sapiens

<400> 21

Met Arg Ala Gln Gly Arg Gly Arg Leu Pro Arg Arg Leu Leu Leu 1 5 10 15

Leu Ala Leu Trp Val Gln Ala Ala Arg Pro Met Gly Tyr Phe Glu Leu 20 25 30

Gln Leu Ser Ala Leu Arg Asn Val Asn Gly Glu Leu Leu Ser Gly Ala 35 40 45

Cys Cys Asp Gly Asp Gly Arg Thr Thr Arg Ala Gly Gly Cys Gly His 50 60

Asp Glu Cys Asp Thr Tyr Val Arg Val Cys Leu Lys Glu Tyr Gln Ala 65 70 75 80

Lys Val Thr Pro Thr Gly Pro Cys Ser Tyr Gly His Gly Ala Thr Pro 85 90 95

Val Leu Gly Gly Asn Ser Phe Tyr Leu Pro Pro Ala Gly Ala Ala Gly
100 105 110

Asp Arg Ala Arg Ala Arg Ala Gly Gly Asp Gln Asp Pro Gly 115 120 125

Leu Val Val Ile Pro Phe Gln Phe Ala Trp Pro Arg Ser Phe Thr Leu 130 135 140

Ile Val Glu Ala Trp Asp Trp Asp Asn Asp Thr Thr Pro Asn Glu Glu 145 150 155 160

Leu Leu Ile Glu Arg Val Ser His Ala Gly Met Ile Asn Pro Glu Asp 165 170 175

Arg Trp Lys Ser Leu His Phe Ser Gly His Val Ala His Leu Glu Leu 180 185 190

Gln Ile Arg Val Arg Cys Asp Glu Asn Tyr Tyr Ser Ala Thr Cys Asn 195 200 205

Lys Phe Cys Arg Pro Arg Asn Asp Phe Phe Gly His Tyr Thr Cys Asp Gln Tyr Gly Asn Lys Ala Cys Met Asp Gly Trp Met Gly Lys Glu Cys 230 Lys Glu Ala Val Cys Lys Gln Gly Cys Asn Leu Leu His Gly Gly Cys 250 Thr Val Pro Gly Glu Cys Arg Cys Ser Tyr Gly Trp Gln Gly Arg Phe Cys Asp Glu Cys Val Pro Tyr Pro Gly Cys Val His Gly Ser Cys Val Glu Pro Trp Gln Cys Asn Cys Glu Thr Asn Trp Gly Gly Leu Leu Cys 295 Asp Lys Asp Leu Asn Tyr Cys Gly Ser His His Pro Cys Thr Asn Gly 315 Gly Thr Cys Ile Asn Ala Glu Pro Asp Gln Tyr Arg Cys Thr Cys Pro Asp Gly Tyr Ser Gly Arg Asn Cys Glu Lys Ala Glu His Ala Cys Thr 340 Ser Asn Pro Cys Ala Asn Gly Gly Ser Cys His Glu Val Pro Ser Gly 360 Phe Glu Cys His Cys Pro Ser Gly Trp Ser Gly Pro Thr Cys Ala Leu Asp Ile Asp Glu Cys Ala Ser Asn Pro Cys Ala Ala Gly Gly Thr Cys 395 Val Asp Gln Val Asp Gly Phe Glu Cys Ile Cys Pro Glu Gln Trp Val Gly Ala Thr Cys Gln Leu Asp Ala Asn Glu Cys Glu Gly Lys Pro Cys 425 Leu Asn Ala Phe Ser Cys Lys Asn Leu Ile Gly Gly Tyr Tyr Cys Asp Cys Ile Pro Gly Trp Lys Gly Ile Asn Cys His Ile Asn Val Asn Asp

Cys Arg Gly Gln Cys Gln His Gly Gly Thr Cys Lys Asp Leu Val Asn 480

Gly Tyr Gln Cys Val Cys Pro Arg Gly Phe Gly Gly Arg His Cys Glu 495

Leu Glu Arg Asp Lys Cys Ala Ser Ser Pro Cys His Ser Gly Gly Leu 510

Cys Glu Asp Leu Ala Asp Gly Phe His Cys His Cys Pro Gln Gly Phe 515 520 525

Ser Gly Pro Leu Cys Glu Val Asp Val Asp Leu Cys Glu Pro Ser Pro 530 535 540

Cys Arg Asn Gly Ala Arg Cys Tyr Asn Leu Glu Gly Asp Tyr Tyr Cys 545 550 555 560

Ala Cys Pro Asp Asp Phe Gly Gly Lys Asn Cys Ser Val Pro Arg Glu 565 570 575

Pro Cys Pro Gly Gly Ala Cys Arg Val Ile Asp Gly Cys Gly Ser Asp 580 585 590

Ala Gly Pro Gly Met Pro Gly Thr Ala Ala Ser Gly Val Cys Gly Pro 595 600 605

His Gly Arg Cys Val Ser Gln Pro Gly Gly Asn Phe Ser Cys Ile Cys 610 620

Asp Ser Gly Phe Thr Gly Thr Tyr Cys His Glu Asn Ile Asp Asp Cys 625 630 635 640

Leu Gly Gln Pro Cys Arg Asn Gly Gly Thr Cys Ile Asp Glu Val Asp 645 650 655

Ala Phe Arg Cys Phe Cys Pro Ser Gly Trp Glu Gly Glu Leu Cys Asp 660 665 670

Thr Asn Pro Asn Asp Cys Leu Pro Asp Pro Cys His Ser Arg Gly Arg 675 680 685

Cys Tyr Asp Leu Val Asn Asp Phe Tyr Cys Ala Cys Asp Asp Gly Trp 690 695 700

Lys Gly Lys Thr Cys His Ser Arg Glu Phe Gln Cys Asp Ala Tyr Thr 705 710 715 720

Cys Ser Asn Gly Gly Thr Cys Tyr Asp Ser Gly Asp Thr Phe Arg Cys
725 730 735

Ala Cys Pro Pro Gly Trp Lys Gly Ser Thr Cys Ala Val Ala Lys Asn
740 745 750

Ser Ser Cys Leu Pro Asn Pro Cys Val Asn Gly Gly Thr Cys Val Gly 755 760 765

Ser Gly Ala Ser Phe Ser Cys Ile Cys Arg Asp Gly Trp Glu Gly Arg 770 775 780

Thr Cys Thr His Asn Thr Asn Asp Cys Asn Pro Leu Pro Cys Tyr Asn 785 790 795 800

Gly Gly Ile Cys Val Asp Gly Val Asn Trp Phe Arg Cys Glu Cys Ala 805 810 815

- Pro Gly Phe Ala Gly Pro Asp Cys Arg Ile Asn Ile Asp Glu Cys Gln 820 825 830
- Ser Ser Pro Cys Ala Tyr Gly Ala Thr Cys Val Asp Glu Ile Asn Gly 835 840
- Tyr Arg Cys Ser Cys Pro Pro Gly Arg Ala Gly Pro Arg Cys Gln Glu 850 855 860
- Val Ile Gly Phe Gly Arg Ser Cys Trp Ser Arg Gly Thr Pro Phe Pro 865 870 875 880
- His Gly Ser Ser Trp Val Glu Asp Cys Asn Ser Cys Arg Cys Leu Asp 885 890 895
- Gly Arg Arg Asp Cys Ser Lys Val Trp Cys Gly Trp Lys Pro Cys Leu 900 905 910
- Leu Ala Gly Gln Pro Glu Ala Leu Ser Ala Gln Cys Pro Leu Gly Gln 915 920 925
- Arg Cys Leu Glu Lys Ala Pro Gly Gln Cys Leu Arg Pro Pro Cys Glu 930 940
- Ala Trp Gly Glu Cys Gly Ala Glu Glu Pro Pro Ser Thr Pro Cys Leu 945 950 955 960
- Pro Arg Ser Gly His Leu Asp Asn Asn Cys Ala Arg Leu Thr Leu His 965 970 975
- Phe Asn Arg Asp His Val Pro Gln Gly Thr Thr Val Gly Ala Ile Cys 980 985 990
- Ser Gly Ile Arg Ser Leu Pro Ala Thr Arg Ala Val Ala Arg Asp Arg 995 1000 1005
- Leu Leu Val Leu Cys Asp Arg Ala Ser Ser Gly Ala Ser Ala Val 1010 1015 1020
- Glu Val Ala Val Ser Phe Ser Pro Ala Arg Asp Leu Pro Asp Ser Ser 1025 1030 1035 1040
- Leu Ile Gln Gly Ala Ala His Ala Ile Val Ala Ala Ile Thr Gln Arg 1045 1050 1055
- Gly Asn Ser Ser Leu Leu Leu Ala Val Thr Glu Val Lys Val Glu Thr 1060 1065 1070
- Val Val Thr Gly Gly Ser Ser Thr Gly Leu Leu Val Pro Val Leu Cys 1075 1080 1085
- Gly Ala Phe Ser Val Leu Trp Leu Ala Cys Val Val Leu Cys Val Trp 1090 1095 1100
- Trp Thr Arg Lys Arg Arg Lys Glu Arg Glu Arg Ser Arg Leu Pro Arg 1105 1110 1115 1120

Glu Glu Ser Ala Asn Asn Gln Trp Ala Pro Leu Asn Pro Ile Arg Asn 1125 1130 1135

Pro Ile Glu Arg Pro Gly Gly His Lys Asp Val Leu Tyr Gln Cys Lys 1140 1145 1150

Asn Phe Thr Pro Pro Pro Arg Arg Ala Asp Glu Ala Leu Pro Gly Pro 1155 1160 1165

Ala Gly His Ala Ala Val Arg Glu Asp Glu Glu Asp Glu Asp Leu Gly 1170 1175 1180

Arg Gly Glu Glu Asp Ser Leu Glu Ala Glu Lys Phe Leu Ser His Lys 1185 1190 1195 1200

Phe Thr Lys Asp Pro Gly Arg Ser Pro Gly Arg Pro Ala His Trp Ala 1205 1210 1215

Ser Gly Pro Lys Val Asp Asn Arg Ala Val Arg Ser Ile Asn Glu Ala 1220 1225 1230

Arg Tyr Ala Gly Lys Glu 1235

<210> 22

<211> 2556

<212> PRT

<213> Homo sapiens

<220>

<221> MOD_RES

<222> (891)

<223> Variable amino acid

<400> 22

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Leu Ala Arg Gly Pro Arg Cys Ser Gln Pro Gly Glu Thr Cys Leu 20 25 30

Asn Gly Gly Lys Cys Glu Ala Ala Asn Gly Thr Glu Ala Cys Val Cys 35 40 45

Gly Gly Ala Phe Val Gly Pro Arg Cys Gln Asp Pro Asn Pro Cys Leu 50 55 60

Ser Thr Pro Cys Lys Asn Ala Gly Thr Cys His Val Val Asp Arg Arg 65 70 75 80

Gly Val Ala Asp Tyr Ala Cys Ser Cys Ala Leu Gly Phe Ser Gly Pro 85 90 95

Leu Cys Leu Thr Pro Leu Asp Asn Ala Cys Leu Thr Asn Pro Cys Arg 100 105 110

- Asn Gly Gly Thr Cys Asp Leu Leu Thr Leu Thr Glu Tyr Lys Cys Arg 115 120 125
- Cys Pro Pro Gly Trp Ser Gly Lys Ser Cys Gln Gln Ala Asp Pro Cys 130 140
- Ala Ser Asn Pro Cys Ala Asn Gly Gly Gln Cys Leu Pro Phe Glu Ala 145 150 155 160
- Ser Tyr Ile Cys His Cys Pro Pro Ser Phe His Gly Pro Thr Cys Arg 165 170 175
- Gln Asp Val Asn Glu Cys Gly Gln Lys Pro Arg Leu Cys Arg His Gly 180 185 190
- Gly Thr Cys His Asn Glu Val Gly Ser Tyr Arg Cys Val Cys Arg Ala 195 200 205
- Thr His Thr Gly Pro Asn Cys Glu Arg Pro Tyr Val Pro Cys Ser Pro 210 215 220
- Ser Pro Cys Gln Asn Gly Gly Thr Cys Arg Pro Thr Gly Asp Val Thr 225 230 235 240
- His Glu Cys Ala Cys Leu Pro Gly Phe Thr Gly Gln Asn Cys Glu Glu
 245 250 255
- Asn Ile Asp Asp Cys Pro Gly Asn Asn Cys Lys Asn Gly Gly Ala Cys 260 265 270
- Val Asp Gly Val Asn Thr Tyr Asn Cys Pro Cys Pro Pro Glu Trp Thr 275 280 285
- Gly Gln Tyr Cys Thr Glu Asp Val Asp Glu Cys Gln Leu Met Pro Asn 290 295 300
- Cys Val Cys Val Asn Gly Trp Thr Gly Glu Asp Cys Ser Glu Asn Ile 325 330 335
- Asp Asp Cys Ala Ser Ala Ala Cys Phe His Gly Ala Thr Cys His Asp 340 345 350
- Arg Val Ala Ser Phe Tyr Cys Glu Cys Pro His Gly Arg Thr Gly Leu 355 360 365
- Leu Cys His Leu Asn Asp Ala Cys Ile Ser Asn Pro Cys Asn Glu Gly 370 375 380
- Ser Asn Cys Asp Thr Asn Pro Val Asn Gly Lys Ala Ile Cys Thr Cys 385 390 395 400
- Pro Ser Gly Tyr Thr Gly Pro Ala Cys Ser Gln Asp Val Asp Glu Cys 405 410 415

Ser Leu Gly Ala Asn Pro Cys Glu His Ala Gly Lys Cys Ile Asn Thr 425 Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln Gly Tyr Thr Gly Pro Arg Cys Glu Ile Asp Val Asn Glu Cys Val Ser Asn Pro Cys Gln Asn Asp Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe Gln Cys Met Cys Met Pro Gly Tyr Glu Gly Val His Cys Glu Val Asn Thr Asp Glu Cys Ala Ser Ser Pro Cys Leu His Asn Gly Arg Cys Leu Asp Lys Ile Asn Glu Phe Gln Cys Glu Cys Pro Thr Gly Phe Thr Gly His Leu Cys Gln Tyr Asp 520 Val Asp Glu Cys Ala Ser Thr Pro Cys Lys Asn Gly Ala Lys Cys Leu Asp Gly Pro Asn Thr Tyr Thr Cys Val Cys Thr Glu Gly Tyr Thr Gly Thr His Cys Glu Val Asp Ile Asp Glu Cys Asp Pro Asp Pro Cys His Tyr Gly Ser Cys Lys Asp Gly Val Ala Thr Phe Thr Cys Leu Cys Arg Pro Gly Tyr Thr Gly His His Cys Glu Thr Asn Ile Asn Glu Cys Ser Ser Gln Pro Cys Arg Leu Arg Gly Thr Cys Gln Asp Pro Asp Asn Ala Tyr Leu Cys Phe Cys Leu Lys Gly Thr Thr Gly Pro Asn Cys Glu Ile 635 Asn Leu Asp Asp Cys Ala Ser Ser Pro Cys Asp Ser Gly Thr Cys Leu Asp Lys Ile Asp Gly Tyr Glu Cys Ala Cys Glu Pro Gly Tyr Thr Gly Ser Met Cys Asn Ser Asn Ile Asp Glu Cys Ala Gly Asn Pro Cys His 680 Asn Gly Gly Thr Cys Glu Asp Gly Ile Asn Gly Phe Thr Cys Arg Cys 690 Pro Glu Gly Tyr His Asp Pro Thr Cys Leu Ser Glu Val Asn Glu Cys 710

- Asn Ser Asn Pro Cys Val His Gly Ala Cys Arg Asp Ser Leu Asn Gly
 725 730 735
- Tyr Lys Cys Asp Cys Asp Pro Gly Trp Ser Gly Thr Asn Cys Asp Ile
 740 745 750
- Asn Asn Glu Cys Glu Ser Asn Pro Cys Val Asn Gly Gly Thr Cys
 755 760 765
- Lys Asp Met Thr Ser Gly Ile Val Cys Thr Cys Arg Glu Gly Phe Ser 770 780
- Gly Pro Asn Cys Gln Thr Asn Ile Asn Glu Cys Ala Ser Asn Pro Cys 785 790 795 800
- Leu Asn Lys Gly Thr Cys Ile Asp Asp Val Ala Gly Tyr Lys Cys Asn 805 810 815
- Cys Leu Leu Pro Tyr Thr Gly Ala Thr Cys Glu Val Val Leu Ala Pro 820 825 830
- Cys Ala Pro Ser Pro Cys Arg Asn Gly Gly Glu Cys Arg Gln Ser Glu 835 840 845
- Asp Tyr Glu Ser Phe Ser Cys Val Cys Pro Thr Ala Gly Ala Lys Gly 850 855 860
- Gln Thr Cys Glu Val Asp Ile Asn Glu Cys Val Leu Ser Pro Cys Arg 865 870 875 880
- His Gly Ala Ser Cys Gln Asn Thr His Gly Xaa Tyr Arg Cys His Cys 885 890 895
- Gln Ala Gly Tyr Ser Gly Arg Asn Cys Glu Thr Asp Ile Asp Asp Cys 900 905 910
- Arg Pro Asn Pro Cys His Asn Gly Gly Ser Cys Thr Asp Gly Ile Asn 915 920 925
- Thr Ala Phe Cys Asp Cys Leu Pro Gly Phe Arg Gly Thr Phe Cys Glu 930 935 940
- Glu Asp Ile Asn Glu Cys Ala Ser Asp Pro Cys Arg Asn Gly Ala Asn 945 950 955 960
- Cys Thr Asp Cys Val Asp Ser Tyr Thr Cys Thr Cys Pro Ala Gly Phe 965 970 975
- Ser Gly Ile His Cys Glu Asn Asn Thr Pro Asp Cys Thr Glu Ser Ser 980 985 990
- Cys Phe Asn Gly Gly Thr Cys Val Asp Gly Ile Asn Ser Phe Thr Cys 995 1000 1005
- Leu Cys Pro Pro Gly Phe Thr Gly Ser Tyr Cys Gln His Val Val Asn 1010 1015 1020

- Glu Cys Asp Ser Arg Pro Cys Leu Leu Gly Gly Thr Cys Gln Asp Gly 1025 1030 1035 1040
- Arg Gly Leu His Arg Cys Thr Cys Pro Gln Gly Tyr Thr Gly Pro Asn 1045 1050 1055
- Cys Gln Asn Leu Val His Trp Cys Asp Ser Ser Pro Cys Lys Asn Gly
 1060 1065 1070
- Gly Lys Cys Trp Gln Thr His Thr Gln Tyr Arg Cys Glu Cys Pro Ser 1075 1080 1085
- Gly Trp Thr Gly Leu Tyr Cys Asp Val Pro Ser Val Ser Cys Glu Val 1090 1095 1100
- Ala Ala Gln Arg Gln Gly Val Asp Val Ala Arg Leu Cys Gln His Gly 1105 1110 1115 1120
- Gly Leu Cys Val Asp Ala Gly Asn Thr His His Cys Arg Cys Gln Ala 1125 1130 1135
- Gly Tyr Thr Gly Ser Tyr Cys Glu Asp Leu Val Asp Glu Cys Ser Pro 1140 1145 1150
- Ser Pro Cys Gln Asn Gly Ala Thr Cys Thr Asp Tyr Leu Gly Gly Tyr 1155 1160 1165
- Ser Cys Lys Cys Val Ala Gly Tyr His Gly Val Asn Cys Ser Glu Glu 1170 1175 1180
- Ile Asp Glu Cys Leu Ser His Pro Cys Gln Asn Gly Gly Thr Cys Leu 1185 1190 1195 1200
- Asp Leu Pro Asn Thr Tyr Lys Cys Ser Cys Pro Arg Gly Thr Gln Gly
 1205 1210 1215
- Val His Cys Glu Ile Asn Val Asp Asp Cys Asn Pro Pro Val Asp Pro 1220 1225 1230
- Val Ser Arg Ser Pro Lys Cys Phe Asn Asn Gly Thr Cys Val Asp Gln 1235 1240 1245
- Val Gly Gly Tyr Ser Cys Thr Cys Pro Pro Gly Phe Val Gly Glu Arg 1250 1255 1260
- Cys Glu Gly Asp Val Asn Glu Cys Leu Ser Asn Pro Cys Asp Ala Arg 1265 1270 1275 1280
- Gly Thr Gln Asn Cys Val Gln Arg Val Asn Asp Phe His Cys Glu Cys 1285 1290 1295
- Arg Ala Gly His Thr Gly Arg Arg Cys Glu Ser Val Ile Asn Gly Cys 1300 1305 1310
- Lys Gly Lys Pro Cys Lys Asn Gly Gly Thr Cys Ala Val Ala Ser Asn 1315 1320 1325

- Thr Ala Arg Gly Phe Ile Cys Lys Cys Pro Ala Gly Phe Glu Gly Ala 1330 1335 1340
- Thr Cys Glu Asn Asp Ala Arg Thr Cys Gly Ser Leu Arg Cys Leu Asn 1345 1350 1355 1360
- Gly Gly Thr Cys Ile Ser Gly Pro Arg Ser Pro Thr Cys Leu Cys Leu 1365 1370 1375
- Gly Pro Phe Thr Gly Pro Glu Cys Gln Phe Pro Ala Ser Ser Pro Cys 1380 1385 1390
- Leu Gly Gly Asn Pro Cys Tyr Asn Gln Gly Thr Cys Glu Pro Thr Ser 1395 1400 1405
- Glu Ser Pro Phe Tyr Arg Cys Leu Cys Pro Ala Lys Phe Asn Gly Leu 1410 1415 1420
- Leu Cys His Ile Leu Asp Tyr Ser Phe Gly Gly Gly Ala Gly Arg Asp 1425 1430 1435 1440
- Ile Pro Pro Pro Leu Ile Glu Glu Ala Cys Glu Leu Pro Glu Cys Gln
 1445 1450 1455
- Glu Asp Ala Gly Asn Lys Val Cys Ser Leu Gln Cys Asn Asn His Ala 1460 1465 1470
- Cys Gly Trp Asp Gly Gly Asp Cys Ser Leu Asn Phe Asn Asp Pro Trp 1475 1480 1485
- Lys Asn Cys Thr Gln Ser Leu Gln Cys Trp Lys Tyr Phe Ser Asp Gly 1490 1495 1500
- His Cys Asp Ser Gln Cys Asn Ser Ala Gly Cys Leu Phe Asp Gly Phe 1505 1510 1515 1520
- Asp Cys Gln Arg Ala Glu Gly Gln Cys Asn Pro Leu Tyr Asp Gln Tyr
 1525 1530 1535
- Cys Lys Asp His Phe Ser Asp Gly His Cys Asp Gln Gly Cys Asn Ser 1540 1545 1550
- Ala Glu Cys Glu Trp Asp Gly Leu Asp Cys Ala Glu His Val Pro Glu 1555 1560 1565
- Arg Leu Ala Ala Gly Thr Leu Val Val Val Leu Met Pro Pro Glu 1570 1580
- Gln Leu Arg Asn Ser Ser Phe His Phe Leu Arg Glu Leu Ser Arg Val 1585 1590 1595 1600
- Leu His Thr Asn Val Val Phe Lys Arg Asp Ala His Gly Gln Gln Met 1605 1610 1615
- Ile Phe Pro Tyr Tyr Gly Arg Glu Glu Glu Leu Arg Lys His Pro Ile 1620 1625 1630

- Lys Arg Ala Ala Glu Gly Trp Ala Ala Pro Asp Ala Leu Leu Gly Gln 1635 1640 1645
- Val Lys Ala Ser Leu Leu Pro Gly Gly Ser Glu Gly Gly Arg Arg Arg 1650 1655 1660
- Arg Glu Leu Asp Pro Met Asp Val Arg Gly Ser Ile Val Tyr Leu Glu 1665 1670 1680
- Ile Asp Asn Arg Gln Cys Val Gln Ala Ser Ser Gln Cys Phe Gln Ser 1685 1690 1695
- Ala Thr Asp Val Ala Ala Phe Leu Gly Ala Leu Ala Ser Leu Gly Ser 1700 1705 1710
- Leu Asn Ile Pro Tyr Lys Ile Glu Ala Val Gln Ser Glu Thr Val Glu 1715 1720 1725
- Pro Pro Pro Pro Ala Gln Leu His Phe Met Tyr Val Ala Ala Ala 1730 1740
- Phe Val Leu Leu Phe Phe Val Gly Cys Gly Val Leu Leu Ser Arg Lys 1745 1750 1755 . 1760
- Arg Arg Arg Gln His Gly Gln Leu Trp Phe Pro Glu Gly Phe Lys Val 1765 1770 1775
- Ser Glu Ala Ser Lys Lys Lys Arg Glu Pro Leu Gly Glu Asp Ser 1780 1785 1790
- Val Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp Gly Ala Leu Met Asp 1795 1800 1805
- Asp Asn Gln Asn Glu Trp Gly Asp Glu Asp Leu Glu Thr Lys Lys Phe 1810 1815 1820
- Arg Phe Glu Glu Pro Val Val Leu Pro Asp Leu Asp Asp Gln Thr Asp 1825 1830 1835 1840
- His Arg Gln Trp Thr Gln Gln His Leu Asp Ala Ala Asp Leu Arg Met 1845 1850 1855
- Ser Ala Met Ala Pro Thr Pro Pro Gln Gly Glu Val Asp Ala Asp Cys 1860 1865 1870
- Met Asp Val Asn Val Arg Gly Pro Asp Gly Phe Thr Pro Leu Met Ile 1875 1880 1885
- Ala Ser Cys Ser Gly Gly Gly Leu Glu Thr Gly Asn Ser Glu Glu Glu 1890 1895 1900
- Glu Asp Ala Pro Ala Val Ile Ser Asp Phe Ile Tyr Gln Gly Ala Ser 1905 1910 1915 1920
- Leu His Asn Gln Thr Asp Arg Thr Gly Glu Thr Ala Leu His Leu Ala 1925 1930 1935

- Ala Arg Tyr Ser Arg Ser Asp Ala Ala Lys Arg Leu Leu Glu Ala Ser 1940 1945 1950
- Ala Asp Ala Asn Ile Gln Asp Asn Met Gly Arg Thr Pro Leu His Ala 1955 1960 1965
- Ala Val Ser Ala Asp Ala Gln Gly Val Phe Gln Ile Leu Ile Arg Asn 1970 1975 1980
- Arg Ala Thr Asp Leu Asp Ala Arg Met His Asp Gly Thr Thr Pro Leu 1985 1990 1995 2000
- Ile Leu Ala Ala Arg Leu Ala Val Glu Gly Met Leu Glu Asp Leu Ile 2005 2010 2015
- Asn Ser His Ala Asp Val Asn Ala Val Asp Asp Leu Gly Lys Ser Ala 2020 2025 2030
- Leu His Trp Ala Ala Ala Val Asn Asn Val Asp Ala Ala Val Val Leu 2035 2040 2045
- Leu Lys Asn Gly Ala Asn Lys Asp Met Gln Asn Asn Arg Glu Glu Thr 2050 2060
- Pro Leu Phe Leu Ala Ala Arg Glu Gly Ser Tyr Glu Thr Ala Lys Val 2065 2070 2075 2080
- Leu Leu Asp His Phe Ala Asn Arg Asp Ile Thr Asp His Met Asp Arg 2085 2090 2095
- Leu Pro Arg Asp Ile Ala Gln Glu Arg Met His His Asp Ile Val Arg 2100 2105 2110
- Leu Leu Asp Glu Tyr Asn Leu Val Arg Ser Pro Gln Leu His Gly Ala 2115 2120 2125
- Pro Leu Gly Gly Thr Pro Thr Leu Ser Pro Pro Leu Cys Ser Pro Asn 2130 2135 2140
- Gly Tyr Leu Gly Ser Leu Lys Pro Gly Val Gln Gly Lys Lys Val Arg 2145 2150 2155 2160
- Lys Pro Ser Ser Lys Gly Leu Ala Cys Gly Ser Lys Glu Ala Lys Asp 2165 2170 2175
- Leu Lys Ala Arg Arg Lys Lys Ser Gln Asp Gly Lys Gly Cys Leu Leu 2180 2185 2190
- Asp Ser Ser Gly Met Leu Ser Pro Val Asp Ser Leu Glu Ser Pro His 2195 2200 2205
- Gly Tyr Leu Ser Asp Val Ala Ser Pro Pro Leu Leu Pro Ser Pro Phe 2210 2215 2220
- Gln Gln Ser Pro Ser Val Pro Leu Asn His Leu Pro Gly Met Pro Asp 2225 2230 2235 2240

- Thr His Leu Gly Ile Gly His Leu Asn Val Ala Ala Lys Pro Glu Met 2245 2250 2255
- Ala Ala Leu Gly Gly Gly Arg Leu Ala Phe Glu Thr Gly Pro Pro 2260 2265 2270
- Arg Leu Ser His Leu Pro Val Ala Ser Gly Thr Ser Thr Val Leu Gly 2275 2280 2285
- Ser Ser Ser Gly Gly Ala Leu Asn Phe Thr Val Gly Gly Ser Thr Ser 2290 2295 2300
- Leu Asn Gly Gln Cys Glu Trp Leu Ser Arg Leu Gln Ser Gly Met Val 2305 2310 2315 2320
- Pro Asn Gln Tyr Asn Pro Leu Arg Gly Ser Val Ala Pro Gly Pro Leu 2325 2330 2335
- Ser Thr Gln Ala Pro Ser Leu Gln His Gly Met Val Gly Pro Leu His 2340 2345 2350
- Ser Ser Leu Ala Ala Ser Ala Leu Ser Gln Met Met Ser Tyr Gln Gly 2355 2360 2365
- Leu Pro Ser Thr Arg Leu Ala Thr Gln Pro His Leu Val Gln Thr Gln 2370 2380
- Gln Val Gln Pro Gln Asn Leu Gln Met Gln Gln Gln Asn Leu Gln Pro 2385 2390 2395 2400
- Ala Asn Ile Gln Gln Gln Ser Leu Gln Pro Pro Pro Pro Pro Pro 2405 2410 2415
- Gln Pro His Leu Gly Val Ser Ser Ala Ala Ser Gly His Leu Gly Arg 2420 2425 2430
- Ser Phe Leu Ser Gly Glu Pro Ser Gln Ala Asp Val Gln Pro Leu Gly 2435 2440 2445
- Pro Ser Ser Leu Ala Val His Thr Ile Leu Pro Gln Glu Ser Pro Ala 2450 2455 2460
- Leu Pro Thr Ser Leu Pro Ser Ser Leu Val Pro Pro Val Thr Ala Ala 2465 2470 2475 2480
- Gln Phe Leu Thr Pro Pro Ser Gln His Ser Tyr Ser Ser Pro Val Asp 2485 2490 2495
- Asn Thr Pro Ser His Gln Leu Gln Val Pro Glu His Pro Phe Leu Thr 2500 2505 2510
- Pro Ser Pro Glu Ser Pro Asp Gln Trp Ser Ser Ser Pro His Ser 2515 2520 2525
- Asn Val Ser Asp Trp Ser Glu Gly Val Ser Ser Pro Pro Thr Ser Met 2530 2540

Gln Ser Gln Ile Ala Arg Ile Pro Glu Ala Phe Lys 2545 2550 2555

<210> 23

<211> 2471

<212> PRT

<213> Homo sapiens

<400> 23

Met Pro Ala Leu Arg Pro Ala Leu Leu Trp Ala Leu Leu Ala Leu Trp 1 5 10 15

Leu Cys Cys Ala Ala Pro Ala His Ala Leu Gln Cys Arg Asp Gly Tyr
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Glu Pro Cys Val Asn Glu Gly Met Cys Val Thr Tyr His Asn Gly Thr 35 40 45

Gly Tyr Cys Lys Cys Pro Glu Gly Phe Leu Gly Glu Tyr Cys Gln His 50 55

Arg Asp Pro Cys Glu Lys Asn Arg Cys Gln Asn Gly Gly Thr Cys Val 65 70 75 80

Ala Gln Ala Met Leu Gly Lys Ala Thr Cys Arg Cys Ala Ser Gly Phe 85 90 95

Thr Gly Glu Asp Cys Gln Tyr Ser Thr Ser His Pro Cys Phe Val Ser 100 105 110

Arg Pro Cys Leu Asn Gly Gly Thr Cys His Met Leu Ser Arg Asp Thr 115 120 125

Tyr Glu Cys Thr Cys Gln Val Gly Phe Thr Gly Lys Glu Cys Gln Trp 130 135 140

Thr Asp Ala Cys Leu Ser His Pro Cys Ala Asn Gly Ser Thr Cys Thr 145 150 155 160

Thr Val Ala Asn Gln Phe Ser Cys Lys Cys Leu Thr Gly Phe Thr Gly
165 170 175

Gln Lys Cys Glu Thr Asp Val Asn Glu Cys Asp Ile Pro Gly His Cys 180 185 190

Gln His Gly Gly Thr Cys Leu Asn Leu Pro Gly Ser Tyr Gln Cys Gln 195 200 205

Cys Pro Gln Gly Phe Thr Gly Gln Tyr Cys Asp Ser Leu Tyr Val Pro 210 215 220

Cys Ala Pro Ser Pro Cys Val Asn Gly Gly Thr Cys Arg Gln Thr Gly 225 230 235 240

- Asp Phe Thr Phe Glu Cys Asn Cys Leu Pro Gly Phe Glu Gly Ser Thr 245 250 255
- Cys Glu Arg Asn Ile Asp Asp Cys Pro Asn His Arg Cys Gln Asn Gly 260 265 270
- Gly Val Cys Val Asp Gly Val Asn Thr Tyr Asn Cys Arg Cys Pro Pro 275 280 285
- Gln Trp Thr Gly Gln Phe Cys Thr Glu Asp Val Asp Glu Cys Leu Leu 290 295 300
- Gln Pro Asn Ala Cys Gln Asn Gly Gly Thr Cys Ala Asn Arg Asn Gly 305 310 315 320
- Gly Tyr Gly Cys Val Cys Val Asn Gly Trp Ser Gly Asp Asp Cys Ser 325 330 335
- Glu Asn Ile Asp Asp Cys Ala Phe Ala Ser Cys Thr Pro Gly Ser Thr 340 345 350
- Cys Ile Asp Arg Val Ala Ser Phe Ser Cys Met Cys Pro Glu Gly Lys 355 360 365
- Ala Gly Leu Cys His Leu Asp Asp Ala Cys Ile Ser Asn Pro Cys 370 375 380
- His Lys Gly Ala Leu Cys Asp Thr Asn Pro Leu Asn Gly Gln Tyr Ile 385 390 395 400
- Cys Thr Cys Pro Gln Gly Tyr Lys Gly Ala Asp Cys Thr Glu Asp Val 405 410 415
- Asp Glu Cys Ala Met Ala Asn Ser Asn Pro Cys Glu His Ala Gly Lys 420 425 430
- Cys Val Asn Thr Asp Gly Ala Phe His Cys Glu Cys Leu Lys Gly Tyr 435 440 445
- Ala Gly Pro Arg Cys Glu Met Asp Ile Asn Glu Cys His Ser Asp Pro 450 455 460
- Cys Gln Asn Asp Ala Thr Cys Leu Asp Lys Ile Gly Gly Phe Thr Cys 465 470 475 480
- Leu Cys Met Pro Gly Phe Lys Gly Val His Cys Glu Leu Glu Ile Asn 485 490 495
- Glu Cys Gln Ser Asn Pro Cys Val Asn Asn Gly Gln Cys Val Asp Lys 500 505 510
- Val Asn Arg Phe Gln Cys Leu Cys Pro Pro Gly Phe Thr Gly Pro Val 515 520 525
- Cys Gln Ile Asp Ile Asp Asp Cys Ser Ser Thr Pro Cys Leu Asn Gly 530 535 540

Ala Lys Cys Ile Asp His Pro Asn Gly Tyr Glu Cys Gln Cys Ala Thr Gly Phe Thr Gly Val Leu Cys Glu Glu Asn Ile Asp Asn Cys Asp Pro Asp Pro Cys His His Gly Gln Cys Gln Asp Gly Ile Asp Ser Tyr Thr 580 Cys Ile Cys Asn Pro Gly Tyr Met Gly Ala Ile Cys Ser Asp Gln Ile Asp Glu Cys Tyr Ser Ser Pro Cys Leu Asn Asp Gly Arg Cys Ile Asp Leu Val Asn Gly Tyr Gln Cys Asn Cys Gln Pro Gly Thr Ser Gly Val Asn Cys Glu Ile Asn Phe Asp Asp Cys Ala Ser Asn Pro Cys Ile His 645 650 Gly Ile Cys Met Asp Gly Ile Asn Arg Tyr Ser Cys Val Cys Ser Pro Gly Phe Thr Gly Gln Arg Cys Asn Ile Asp Ile Asp Glu Cys Ala Ser Asn Pro Cys Arg Lys Gly Ala Thr Cys Ile Asn Gly Val Asn Gly Phe 695 Arg Cys Ile Cys Pro Glu Gly Pro His His Pro Ser Cys Tyr Ser Gln Val Asn Glu Cys Leu Ser Asn Pro Cys Ile His Gly Asn Cys Thr Gly Gly Leu Ser Gly Tyr Lys Cys Leu Cys Asp Ala Gly Trp Val Gly Ile Asn Cys Glu Val Asp Lys Asn Glu Cys Leu Ser Asn Pro Cys Gln Asn Gly Gly Thr Cys Asp Asn Leu Val Asn Gly Tyr Arg Cys Thr Cys Lys Lys Gly Phe Lys Gly Tyr Asn Cys Gln Val Asn Ile Asp Glu Cys Ala Ser Asn Pro Cys Leu Asn Gln Gly Thr Cys Phe Asp Asp Ile Ser Gly 810 Tyr Thr Cys His Cys Val Leu Pro Tyr Thr Gly Lys Asn Cys Gln Thr 825

Val Leu Ala Pro Cys Ser Pro Asn Pro Cys Glu Asn Ala Ala Val Cys

- Lys Glu Ser Pro Asn Phe Glu Ser Tyr Thr Cys Leu Cys Ala Pro Gly 850 855 860
- Trp Gln Gly Gln Arg Cys Thr Ile Asp Ile Asp Glu Cys Ile Ser Lys 865 870 875 880
- Pro Cys Met Asn His Gly Leu Cys His Asn Thr Gln Gly Ser Tyr Met 885 890 895
- Cys Glu Cys Pro Pro Gly Phe Ser Gly Met Asp Cys Glu Glu Asp Ile 900 905 910
- Asp Asp Cys Leu Ala Asn Pro Cys Gln Asn Gly Gly Ser Cys Met Asp 915 920 925
- Gly Val Asn Thr Phe Ser Cys Leu Cys Leu Pro Gly Phe Thr Gly Asp 930 935 940
- Lys Cys Gln Thr Asp Met Asn Glu Cys Leu Ser Glu Pro Cys Lys Asn 945 950 955 960
- Gly Gly Thr Cys Ser Asp Tyr Val Asn Ser Tyr Thr Cys Lys Cys Gln 965 970 975
- Ala Gly Phe Asp Gly Val His Cys Glu Asn Asn Ile Asn Glu Cys Thr 980 985 990
- Glu Ser Ser Cys Phe Asn Gly Gly Thr Cys Val Asp Gly Ile Asn Ser 995 1000 1005
- Phe Ser Cys Leu Cys Pro Val Gly Phe Thr Gly Ser Phe Cys Leu His 1010 1015 1020
- Glu Ile Asn Glu Cys Ser Ser His Pro Cys Leu Asn Glu Gly Thr Cys 1025 1030 1035 1040
- Val Asp Gly Leu Gly Thr Tyr Arg Cys Ser Cys Pro Leu Gly Tyr Thr 1045 1050 1055
- Gly Lys Asn Cys Gln Thr Leu Val Asn Leu Cys Ser Arg Ser Pro Cys 1060 1065 1070
- Lys Asn Lys Gly Thr Cys Val Gln Lys Lys Ala Glu Ser Gln Cys Leu 1075 1080 1085
- Cys Pro Ser Gly Trp Ala Gly Ala Tyr Cys Asp Val Pro Asn Val Ser 1090 1095 1100
- Cys Asp Ile Ala Ala Ser Arg Arg Gly Val Leu Val Glu His Leu Cys 1105 1110 1115 1120
- Gln His Ser Gly Val Cys Ile Asn Ala Gly Asn Thr His Tyr Cys Gln 1125 1130 1135
- Cys Pro Leu Gly Tyr Thr Gly Ser Tyr Cys Glu Glu Gln Leu Asp Glu 1140 1145 1150

- Cys Ala Ser Asn Pro Cys Gln His Gly Ala Thr Cys Ser Asp Phe Ile 1155 1160 1165
- Gly Gly Tyr Arg Cys Glu Cys Val Pro Gly Tyr Gln Gly Val Asn Cys 1170 1175 1180
- Glu Tyr Glu Val Asp Glu Cys Gln Asn Gln Pro Cys Gln Asn Gly Gly 1185 1190 1195 1200
- Thr Cys Ile Asp Leu Val Asn His Phe Lys Cys Ser Cys Pro Pro Gly 1205 1210 1215
- Thr Arg Gly Leu Leu Cys Glu Glu Asn Ile Asp Asp Cys Ala Arg Gly 1220 1225 1230
- Pro His Cys Leu Asn Gly Gly Gln Cys Met Asp Arg Ile Gly Gly Tyr 1235 1240 1245
- Ser Cys Arg Cys Leu Pro Gly Phe Ala Gly Glu Arg Cys Glu Gly Asp 1250 1255 1260
- Ile Asn Glu Cys Leu Ser Asn Pro Cys Ser Ser Glu Gly Ser Leu Asp 1265 1270 1275 1280
- Cys Ile Gln Leu Thr Asn Asp Tyr Leu Cys Val Cys Arg Ser Ala Phe 1285 1290 1295
- Thr Gly Arg His Cys Glu Thr Phe Val Asp Val Cys Pro Gln Met Pro 1300 1305 1310
- Cys Leu Asn Gly Gly Thr Cys Ala Val Ala Ser Asn Met Pro Asp Gly 1315 1320 1325
- Phe Ile Cys Arg Cys Pro Pro Gly Phe Ser Gly Ala Arg Cys Gln Ser 1330 1335 1340
- Ser Cys Gly Gln Val Lys Cys Arg Lys Gly Glu Gln Cys Val His Thr 1345 1350 1355 1360
- Ala Ser Gly Pro Arg Cys Phe Cys Pro Ser Pro Arg Asp Cys Glu Ser 1365 1370 1375
- Gly Cys Ala Ser Ser Pro Cys Gln His Gly Gly Ser Cys His Pro Gln 1380 1385 1390
- Arg Gln Pro Pro Tyr Tyr Ser Cys Gln Cys Ala Pro Pro Phe Ser Gly 1395 1400 1405
- Ser Arg Cys Glu Leu Tyr Thr Ala Pro Pro Ser Thr Pro Pro Ala Thr 1410 1415 1420
- Cys Leu Ser Gln Tyr Cys Ala Asp Lys Ala Arg Asp Gly Val Cys Asp 1425 1430 1435 1440
- Glu Ala Cys Asn Ser His Ala Cys Gln Trp Asp Gly Gly Asp Cys Ser 1445 1450 1455

- Leu Thr Met Glu Asn Pro Trp Ala Asn Cys Ser Ser Pro Leu Pro Cys 1460 1465 1470
- Trp Asp Tyr Ile Asn Asn Gln Cys Asp Glu Leu Cys Asn Thr Val Glu 1475 1480 1485
- Cys Leu Phe Asp Asn Phe Glu Cys Gln Gly Asn Ser Lys Thr Cys Lys 1490 1495 1500
- Tyr Asp Lys Tyr Cys Ala Asp His Phe Lys Asp Asn His Cys Asn Gln 1505 1510 1515 1520
- Gly Cys Asn Ser Glu Glu Cys Gly Trp Asp Gly Leu Asp Cys Ala Ala 1525 1530 1535
- Asp Gln Pro Glu Asn Leu Ala Glu Gly Thr Leu Val Ile Val Val Leu 1540 1545 1550
- Met Pro Pro Glu Gln Leu Leu Gln Asp Ala Arg Ser Phe Leu Arg Ala 1555 1560 1565
- Leu Gly Thr Leu Leu His Thr Asn Leu Arg Ile Lys Arg Asp Ser Gln 1570 1580
- Gly Glu Leu Met Val Tyr Pro Tyr Tyr Gly Glu Lys Ser Ala Ala Met 1585 1590 1595 1600
- Lys Lys Gln Arg Met Thr Arg Arg Ser Leu Pro Gly Glu Gln Glu Gln 1605 1610 1615
- Glu Val Ala Gly Ser Lys Val Phe Leu Glu Ile Asp Asn Arg Gln Cys 1620 1625 1630
- Val Gln Asp Ser Asp His Cys Phe Lys Asn Thr Asp Ala Ala Ala 1635 1640 1645
- Leu Leu Ala Ser His Ala Ile Gln Gly Thr Leu Ser Tyr Pro Leu Val 1650 1660
- Ser Val Val Ser Glu Ser Leu Thr Pro Glu Arg Thr Gln Leu Leu Tyr 1665 1670 1675 1680
- Leu Leu Ala Val Ala Val Ile Ile Leu Phe Ile Ile Leu Leu Gly 1685 1690 1695
- Val Ile Met Ala Lys Arg Lys Arg Lys His Gly Ser Leu Trp Leu Pro 1700 1705 1710
- Glu Gly Phe Thr Leu Arg Arg Asp Ala Ser Asn His Lys Arg Arg Glu 1715 1720 1725
- Pro Val Gly Gln Asp Ala Val Gly Leu Lys Asn Leu Ser Val Gln Val 1730 1735 1740
- Ser Glu Ala Asn Leu Ile Gly Thr Gly Thr Ser Glu His Trp Val Asp 1745 1750 1755 1760

- Asp Glu Gly Pro Gln Pro Lys Lys Val Lys Ala Glu Asp Glu Ala Leu 1765 1770 1775
- Leu Ser Glu Glu Asp Asp Pro Ile Asp Arg Pro Trp Thr Gln Gln 1780 1785 1790
- His Leu Glu Ala Ala Asp Ile Arg Arg Thr Pro Ser Leu Ala Leu Thr 1795 1800 1805
- Pro Pro Gln Ala Glu Gln Glu Val Asp Val Leu Asp Val Asn Val Arg 1810 1815 1820
- Gly Pro Asp Gly Cys Thr Pro Leu Met Leu Ala Ser Leu Arg Gly Gly 1825 1830 1835 1840
- Ser Ser Asp Leu Ser Asp Glu Asp Glu Asp Ala Glu Asp Ser Ser Ala 1845 1850 1855
- Asn Ile Ile Thr Asp Leu Val Tyr Gln Gly Ala Ser Leu Gln Ala Gln 1860 1865 1870
- Thr Asp Arg Thr Gly Glu Met Ala Leu His Leu Ala Ala Arg Tyr Ser 1875 1880 1885
- Arg Ala Asp Ala Ala Lys Arg Leu Leu Asp Ala Gly Ala Asp Ala Asn 1890 . 1895 . 1900
- Ala Gln Asp Asn Met Gly Arg Cys Pro Leu His Ala Ala Val Ala Ala 1905 1910 1915 1920
- Asp Ala Gln Gly Val Phe Gln Ile Leu Ile Arg Asn Arg Val Thr Asp 1925 1930 1935
- Leu Asp Ala Arg Met Asn Asp Gly Thr Thr Pro Leu Ile Leu Ala Ala 1940 1945 1950
- Arg Leu Ala Val Glu Gly Met Val Ala Glu Leu Ile Asn Cys Gln Ala 1955 1960 1965
- Asp Val Asn Ala Val Asp Asp His Gly Lys Ser Ala Leu His Trp Ala 1970 1975 1980
- Ala Ala Val Asn Asn Val Glu Ala Thr Leu Leu Leu Leu Lys Asn Gly 1985 1990 1995 2000
- Ala Asn Arg Asp Met Gln Asp Asn Lys Glu Glu Thr Pro Leu Phe Leu 2005 2010 2015
- Ala Ala Arg Glu Gly Ser Tyr Glu Ala Ala Lys Ile Leu Leu Asp His 2020 2025 2030
- Phe Ala Asn Arg Asp Ile Thr Asp His Met Asp Arg Leu Pro Arg Asp 2035 2040 2045
- Val Ala Arg Asp Arg Met His His Asp Ile Val Arg Leu Leu Asp Glu 2050 2055 2060

- Tyr Asn Val Thr Pro Ser Pro Pro Gly Thr Val Leu Thr Ser Ala Leu 2065 2070 2075 2080
- Ser Pro Val Ile Cys Gly Pro Asn Arg Ser Phe Leu Ser Leu Lys His 2085 2090 2095
- Thr Pro Met Gly Lys Lys Ser Arg Arg Pro Ser Ala Lys Ser Thr Met 2100 2105 2110
- Pro Thr Ser Leu Pro Asn Leu Ala Lys Glu Ala Lys Asp Ala Lys Gly 2115 2120 2125
- Ser Arg Arg Lys Lys Ser Leu Ser Glu Lys Val Gln Leu Ser Glu Ser 2130 2135 2140
- Ser Val Thr Leu Ser Pro Val Asp Ser Leu Glu Ser Pro His Thr Tyr 2145 2150 2155 2160
- Val Ser Asp Thr Thr Ser Ser Pro Met Ile Thr Ser Pro Gly Ile Leu 2165 2170 2175
- Gln Ala Ser Pro Asn Pro Met Leu Ala Thr Ala Ala Pro Pro Ala Pro 2180 2185 2190
- Val His Ala Gln His Ala Leu Ser Phe Ser Asn Leu His Glu Met Gln 2195 2200 2205
- Pro Leu Ala His Gly Ala Ser Thr Val Leu Pro Ser Val Ser Gln Leu 2210 2215 2220
- Leu Ser His His His Ile Val Ser Pro Gly Ser Gly Ser Ala Gly Ser 2225 2230 2235 2240
- Leu Ser Arg Leu His Pro Val Pro Val Pro Ala Asp Trp Met Asn Arg 2245 2250 2255
- Met Glu Val Asn Glu Thr Gln Tyr Asn Glu Met Phe Gly Met Val Leu 2260 2265 2270
- Ala Pro Ala Glu Gly Thr His Pro Gly Ile Ala Pro Gln Ser Arg Pro 2275 2280 2285
- Pro Glu Gly Lys His Ile Thr Thr Pro Arg Glu Pro Leu Pro Pro Ile 2290 2295 2300
- Val Thr Phe Gln Leu Ile Pro Lys Gly Ser Ile Ala Gln Pro Ala Gly 2305 2310 2315 2320
- Ala Pro Gln Pro Gln Ser Thr Cys Pro Pro Ala Val Ala Gly Pro Leu 2325 2330 2335
- Pro Thr Met Tyr Gln Ile Pro Glu Met Ala Arg Leu Pro Ser Val Ala 2340 2345 2350
- Phe Pro Thr Ala Met Met Pro Gln Gln Asp Gly Gln Val Ala Gln Thr 2355 2360 2365

Ile Leu Pro Ala Tyr His Pro Phe Pro Ala Ser Val Gly Lys Tyr Pro 2370 2375 2380

Thr Pro Pro Ser Gln His Ser Tyr Ala Ser Ser Asn Ala Ala Glu Arg 2385 2390 2395 2400

Thr Pro Ser His Ser Gly His Leu Gln Gly Glu His Pro Tyr Leu Thr 2405 2410 2415

Pro Ser Pro Glu Ser Pro Asp Gln Trp Ser Ser Ser Pro His Ser 2420 2425 2430

Ala Ser Asp Trp Ser Asp Val Thr Thr Ser Pro Thr Pro Gly Gly Ala 2435 2440 2445

Gly Gly Gln Arg Gly Pro Gly Thr His Met Ser Glu Pro Pro His 2450 2455 2460

Asn Asn Met Gln Val Tyr Ala 2465 2470

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<211> 43

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<223> Variable amino acid

<220>

<221> MOD_RES

<222> (11)..(13)

<223> Variable amino acid

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<221> MOD_RES

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<223> Variable amino acid

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<223> Variable amino acid

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<223> Variable amino acid

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                                  10
20
                              25
Xaa Cys Xaa Xaa Xaa Xaa Xaa Xaa Cys
        35
                           40
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<222> (7)..(9)
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<221> MOD RES

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<223> Acidic or amide amino acid
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<221> MOD_RES
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<222> (37)
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4 1, 1, 1

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<222> (41)..(42)
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Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Xaa Cys Xaa Xaa
25
Xaa Cys Xaa Xaa Xaa Xaa Xaa Xaa Cys
        35
<210> 26
<211> 43
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     preferred DSL domain sequence
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4 P 1 3

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Cys Xaa Xaa Xaa Tyr Tyr Xaa Xaa Xaa Cys Xaa Xaa Xaa Cys Arg Pro
Arg Asx Asp Xaa Phe Gly His Xaa Xaa Cys Xaa Xaa Xaa Gly Xaa Xaa
Xaa Cys Xaa Xaa Gly Trp Xaa Gly Xaa Xaa Cys
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<222> (54)..(138)
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<223> Variable amino acid
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<223> Variable amino acid; this range may encompass 0-21 Xaa repeats
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<222> (175)
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                25
Xaa Xaa Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
            55
90
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa
  130
           135
155
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Gly Xaa Xaa Cys Xaa
       165
<210> 28
<211> 20
<212> DNA
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<223> Description of Artificial Sequence: Primer
<400> 28
gtaacccgtt gaaccccatt
                               20
<210> 29
<211> 20
<212> DNA
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<400> 29
ccatccaatc ggtagtagcg
                               20
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<210> 30
<211> 20
<212> DNA
<213> Artificial Sequence
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<223> Description of Artificial Sequence: Primer
<400> 30
ggtgctgata acagcggaat
                                                                    20
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<211> 20
<212> DNA
<213> Artificial Sequence
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<400> 31
atttttggaa tccttcacgc
                                                                    20
<210> 32
<211> 26
<212> DNA
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<223> Description of Artificial Sequence: Synthetic
      oligonucleotide
<400> 32
gatctggggg gctataaaag ggggta
                                                                    26
<210> 33
<211> 26
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: Synthetic
      oligonucleotide
<400> 33
agcttacccc cttttatagc ccccca
                                                                    26
<210> 34
<211> 50
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<213> Artificial Sequence
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<220>
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      oligonucleotide
<400> 34
gatcccgact cgtgggaaaa tgggcggaag ggcaccgtgg gaaaatagta
                                                                    50
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gatctactat tttcccacgg tgcccttccg cccattttcc cacgagtcgg
                                                                    50
<210> 36
<211> 21
<212> DNA
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<400> 36
caccccatgg ctacctgtca g
                                                                    21
<210> 37
<211> 21
<212> DNA
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<223> Description of Artificial Sequence: Primer
<400> 37
ggctgcacct gctgggtctg c
                                                                   21
<210> 38
<211> 39
<212> DNA
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<223> Description of Artificial Sequence: Primer
aaaggattca ccatggcacg caagcgccgg cgcagtcat
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33

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<210> 39
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Gly Phe Lys Val Ser Glu Ala Ser Lys Lys Lys Arg Arg Glu Pro Leu
Gly Glu Asp Ser Val Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp Gly
Ala Leu Met Asp Asp Asn Gln Asn Glu Trp Gly Asp Glu Asp Leu Glu
Thr Lys Lys Phe Arg Phe Glu Glu Pro Val Val Leu Pro Asp Leu Asp
Asp Gln Thr Asp His Arg Gln Trp Thr Gln Gln His Leu Asp Ala Ala
                                     90
Asp Leu Arg Met Ser Ala Met Ala Pro Thr Pro Pro Gln Gly Glu Val
                                105
Asp Ala Asp Cys Met Asp Val Asn Val Arg Gly Pro Asp Gly Phe Thr
Pro Leu Met Ile Ala Ser Cys Ser Gly Gly Gly Leu Glu Thr Gly Asn
Ser Glu Glu Glu Asp Ala Pro Ala Val Ile Ser Asp Phe Ile Tyr
                    150
Gln Gly Ala Ser Leu His Asn Gln Thr Asp Arg Thr Gly Glu Thr Ala
                165
                                    170
Leu His Leu Ala Ala Arg Tyr Ser Arg Ser Asp Ala Ala Lys Arg Leu
Leu Glu Ala Ser Ala Asp Ala Asn Ile Gln Asp Asn Met Gly Arg Thr
```

195

 Leu 225
 11e Arg Asn Asn Arg 230
 Thr Asp Leu Asp Leu Asp 235
 Arg Arg Met His Asp 240

 Thr Thr Pro Leu 11e Asn Asn Ala Ala Ala Asp 250
 Ala Ash Ala Val Glu Gly Met 255

 Glu Asp Leu 11e Asn Ser His Ala Asp 265
 Val Asn Ala Val Asp Asp Asp Asp Leu 270

 Gly Lys Ser Ala Leu His Trp Ala Ala Ala Val Asn Asn 285
 Val Asn Asn 285

 Ala Val Val Leu Leu Leu Lys Asn Gly Ala Asn Ala Ala Asp 300
 Met Gln Asn Asn 311

 Arg Glu Glu Glu Thr Pro Leu Asp 310
 Phe Leu Ala Ala Arg 315
 Glu Asp Asp 11e Thr Asp 335

 His Met Asp Arg Leu Pro Arg Asp 340
 Phe Ala Asp Arg Asp 12e Thr Asp 335
 Asp Arg Arg Leu Asp 360
 Phe Ala Asp Arg Arg Leu Asp 360
 Asp 345

 Asp 11e Val Arg Arg Leu Leu Asp 360
 Tyr Asn Leu Val Arg Ser Pro Glu 375
 Asp 365
 Pro Chu 375

 Asp 376
 Phe Ala Arg Leu Leu Asp 360
 Phe Ala Arg Arg Leu Val Arg Ser Pro Chu 375
 Phe Ala Ser Pro Arg Arg Ser Pro Chu 375

Pro Leu His Ala Ala Val Ser Ala Asp Ala Gln Gly Val Phe Gln Ile

Gly Cys Leu Leu Asp Ser Ser Gly Met Leu Ser Pro Val Asp Ser Leu 435 440 445

Glu Ser Pro His Gly Tyr Leu Ser Asp Val Ala Ser Pro Pro Leu Leu 450 455

Lys Lys Val Arg Lys Pro Ser Ser Lys Gly Leu Ala Cys Gly Ser Lys

Glu Ala Lys Asp Leu Lys Ala Arg Arg Lys Lys Ser Gln Asp Gly Lys
420
425

Pro Ser Pro Phe Gln Gln Ser Pro Ser Val Pro Leu Asn His Leu Pro 465 470 475 480

Gly Met Pro Asp Thr His Leu Gly Ile Gly His Leu Asn Val Ala Ala 485 490 495

Lys Pro Glu Met Ala Ala Leu Gly Gly Gly Gly Arg Leu Ala Phe Glu 500 505 510

Thr Gly Pro Pro Arg Leu Ser His Leu Pro Val Ala Ser Gly Thr Ser 515 520 525

Thr Val Leu Gly Ser Ser Ser Gly Gly Ala Leu Asn Phe Thr Val Gly 530 540

Gly Ser Thr Ser Leu Asn Gly Gln Cys Glu Trp Leu Ser Arg Leu Gln 545 550 560

Ser Gly Met Val Pro Asn Gln Tyr Asn Pro Leu Arg Gly Ser Val Ala 565 570 575

Pro Gly Pro Leu Ser Thr Gln Ala Pro Ser Leu Gln His Gly Met Val

Gly Pro Leu His Ser Ser Leu Ala Ala Ser Ala Leu Ser Gln Met Met 595 600 605

Ser Tyr Gln Gly Leu Pro Ser Thr Arg Leu Ala Thr Gln Pro His Leu 610 615 620

Val Gln Thr Gln Gln Val Gln Pro Gln Asn Leu Gln Met Gln Gln 625 630 635 640

Asn Leu Gln Pro Ala Asn Ile Gln Gln Gln Gln Ser Leu Gln Pro Pro 645 650 655

Pro Pro Pro Gln Pro His Leu Gly Val Ser Ser Ala Ala Ser Gly 660 665 670

His Leu Gly Arg Ser Phe Leu Ser Gly Glu Pro Ser Gln Ala Asp Val 675 680 685

Gln Pro Leu Gly Pro Ser Ser Leu Ala Val His Thr Ile Leu Pro Gln 690 695 700

Glu Ser Pro Ala Leu Pro Thr Ser Leu Pro Ser Ser Leu Val Pro Pro 705 710 715 720

Val Thr Ala Ala Gln Phe Leu Thr Pro Pro Ser Gln His Ser Tyr Ser 725 730 735

Ser Pro Val Asp Asn Thr Pro Ser His Gln Leu Gln Val Pro Glu His 740 745 750

Pro Phe Leu Thr Pro Ser Pro Glu Ser Pro Asp Gln Trp Ser Ser Ser 755

Ser Pro His Ser Asn Val Ser Asp Trp Ser Glu Gly Val Ser Ser Pro 770 780

Pro Thr Ser Met Gln Ser Gln Ile Ala Arg Ile Pro Glu Ala Phe Lys 785 790 795 800